

CLAIMS

1. A method of identifying a cellular protein involved in the susceptibility to proliferative disease, said method comprising the steps of:

- a) infecting a normal cell and an abnormally proliferating
5 cell with a collection of uncharacterized mutant viruses;
- b) identifying a mutant virus from the collection that can grow in said abnormally proliferating cell and can not grow in said normal cell; and
- c) identifying the mutated viral gene or mutated protein in said virus, which allows said virus to grow on said abnormally proliferating cell; and
10 d) screening to identify the cellular protein which interacts with the wild-type viral protein, but not said mutated viral protein.

2. The method of claim 1, wherein said abnormally proliferating cell is uncharacterized.
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3. The method of claim 1, further comprising identifying a cellular protein that can interact with a wild-type viral protein that corresponds to said mutant viral protein, wherein said cellular protein is not a retinoblastoma tumor suppressor protein.

20 4. The method of claim 3, wherein the step of identifying said cellular protein comprises using an assay that detects protein-protein interactions.

5. The method of claim 4, wherein said assay is a GST-pulldown assay.

25 6. The method of claim 3, further comprising isolating a gene encoding said cellular protein.

7. The method of claim 1, wherein said virus has a mammalian host range.

30 8. The method of claim 7, wherein said mammal is a human.

9. The method of claim 1, wherein said virus is selected from the group consisting of simian virus 40 virus, human polyoma virus, parvovirus, papilloma virus, herpes virus, and primate adenoviruses.

5 10. The method of claim 1, wherein said cellular protein is a tumor suppressor protein.

11. The method of claim 1, wherein said cellular protein is a proto-oncogene product.

10 12. A tumor host range virus isolated using the method of claim 1.

13. A method of determining the presence or absence of an alteration in the genetic material of a cell, said method comprising determining whether a cell can act as a permissive host for the propagation of a characterized T-HR mutant, said T-HR mutant being capable of propagating in an abnormally proliferating cell and not being capable of propagating in a normal cell, wherein said characterized T-HR mutant is unable to propagate in a cell carrying a mutation in the retinoblastoma or p53 gene.

15 20 14. The method of claim 13, wherein the presence of said genetic alteration is indicative of an organism carrying this genetic alteration being at an increased risk of developing a proliferative disease.

25 15. The method of claim 13, wherein said alteration in the genetic material is in a tumor suppressor gene.

16. The method of claim 13, wherein said alteration in the genetic material is in a proto-oncogene.

30 17. The method of claim 13, wherein said characterized T-HR mutant has been characterized as being complemented by a mutation in a specific tumor suppressor gene

or proto-oncogene, wherein said tumor suppressor or proto-oncogene are not the retinoblastoma or p53 gene.

18. The method of claim 13, wherein said cell is a cell from a mammal.

19. The method of claim 18, wherein said mammal is a human.

20. A method of killing an abnormally proliferating cell comprising the steps of:

- (i) contacting an abnormally proliferating cell with a T-HR mutant; and
- (ii) allowing said T-HR mutant to lyse said cell.

21. The method of claim 20, wherein said abnormally proliferating cell is a mammalian cell.

22. The method of claim 21, wherein said mammalian cell is a human cell.

23. The method of claim 20, wherein said abnormally proliferating cell is in a mammal with a proliferative disorder.

24. The method of claim 23, wherein said mammal is a human.

25. The method of claim 20, wherein said T-HR mutant is administered in a pharmaceutically acceptable carrier.

26. The method of claim 20, wherein said T-HR mutant is administered by a method selected from the group consisting of parenteral, intravenous, intraperitoneal, intramuscular, subcutaneous, and subdermal injection.

27. The method of claim 20, wherein said T-HR mutant is administered by a method selected from the group consisting of orally, nasally, topically, and as an aerosol.

